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Serum Perfluoroalkyl Substances in Children Exposed to the World Trade Center Disaster

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Abstract

The World Trade Center (WTC) disaster released large amounts of various chemical substances into the environment, including perfluoroalkyl substances (PFASs). Yet, no studies have examined exposures in children living or attending schools near the disaster site. We measured serum PFASs in WTC Health Registry (WTCHR) respondents who were ≤8 years of age on September 11, 2001 and a sociodemographically-matched comparison group. We also examined the relationship of PFASs levels with dust cloud exposure; home dust exposure, and with traumatic exposure, the latter to take into account differences related to possible mental health consequences and associated behavioral problems. Serum samples, collected between 2014 and 2016, were analyzed from 123 WTCHR participants and from 185 participants in the comparison group. In the WTCHR group, median perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) levels were 1.81 ng/mL and 3.72 ng/mL, respectively. Controlling for sex, caloric intake, race/ethnicity, and date of birth, significant increases among WTCHR participants compared with the

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matched comparison group were detected for perfluorohexanesulfonate (0.23 ng/mL increase or 0.24 log unit increase, p=0.006); PFOS (0.86 ng/mL increase or 0.16 log unit increase, p=0.011); PFOA (0.35 ng/mL increase or 0.18 log unit increase, p<0.001); perfluorononanoic acid (0.12 ng/mL increase or 0.17 log unit increase, p=0.003); perfluorodecanoic acid (0.06 ng/mL increase or 0.42 log unit increase, p<0.001); and perfluoroundecanoic acid (0.03 ng/mL increase or 0.32 log unit increase, p=0.019). Stronger associations were identified for home dust exposures and traumatic exposures than dust cloud. These findings highlight the importance of conducting longitudinal studies in this population to assess possible cardiometabolic and renal consequences related to these exposures.

Keywords

perfluoroalkyl substances; children; World Trade Center disaster; dust cloud; home dust exposure

1. Introduction

The World Trade Center (WTC) disaster released large amounts of particulate matter, heavy metals and persistent organic pollutants (POP). [1] Among various POPs, elevated exposure to perfluoroalkyl substances (PFASs) in personnel responding to the WTC disaster site has been reported among New York State employees and National Guard personnel 5–26 months after the disaster,[2] with a twofold higher concentration of PFOA (mean 8.88 ng/mL) and perfluorohexanesulfonate (PFHxS, mean 3.70 ng/mL) compared to nationally representative samples (4.6 and 1.9 ng/mL, respectively).[2] In addition to acute dust cloud exposures,l-ocal residents experienced significant subchronic exposures from fires and resuspended dust, which entered homes and schools through windows and air shafts.[3] Furthermore, a particular concern remains regarding combustion products released by fires burning for more than 3 months after the event.[1]

PFASs are used as surfactants and stain-resistant coatings on many products, including upholstery, carpet, nonstick cookware,[4, 5] and building and construction material.[6] In addition, PFASs are also found in firefighting material used for fire suppression.[7] Since the disaster, laboratory studies have identified PFASs to disrupt metabolic, cardiovascular and renal functions. PFASs interact with alpha- and gamma-peroxisome proliferator activated receptors, which play key roles in lipid and carbohydrate metabolism.[8] In cell culture studies using the 3T3-L1 preadipocyte system, several PFASs altered gene expression associated with adipocyte differentiation and lipid metabolism,[9] and developmental PFAS exposures in mice have resulted in increased leptin and insulin levels in midlife.[10] Microvascular endothelial cell culture studies have shown that PFAS exposure increases reactive oxidative species and induces endothelial permeability,[11] which plays a critical role in ischemic renal injury.[12] While not all results from experimental studies have been confirmed in humans, some important effects have been reported in human studies. A positive association has been detected between concentrations of perfluorooctanesulfonic acid (PFOS), perfluorooctanoic acid (PFOA) and perfluorononanoic acid (PFNA), and total and non-high-density cholesterol inNational Health and Nutrition Examination Survey (NHANES) participants aged 20–80 years, despite the relatively low level of exposure. [13] In adolescents, PFOA and PFOS have

been found to be significantly associated with dyslipidemia. [14] PFOS and PFNA concentrations have also been shown to be associated with lower levels of insulin growth factor-1 (IGF-1) in children and,[15] among 12–19 year olds in NHANES 2003–2010, those with the highest quartile of serum PFC had significantly lower renal glomerular function compared to those in the lowest quartile,[16] although the possibility of reverse causation cannot be excluded in this cross-sectional study.

A particular concern about early life WTC-related chemical exposure is that childhood represents a uniquely susceptible period for developmental metabolic programming, which can result in adverse health consequences in later life. A previous study examining a population of children with clinical concerns relating to the WTC disaster identified reductions in high density lipoprotein (HDL) and elevations in triglycerides among those with (subchronic) home dust exposure, although in this study no specific chemical compounds were examined.[17] To further examine the plausible role of specific chemical exposures that could potentially contribute to cardiometabolic alterations in exposed children, we compared serum PFAS levels in a sample of WTC-exposed children with levels in a matched comparison group, and to examine the relationship of serum PFAS levels with dust cloud (acute), home dust (subchronic), and traumatic exposures.

2. Methods

2.1 Population

The study population consisted of: (1) a cohort of New York City residents enrolled in the World Trade Center Health Registry (WTCHR) with dates of birth on or between September 11, 1993 and September 10, 2001 and (2) a comparison cohort of individuals born during the same time period, who were ineligible for enrollment in the WTCHR because they either did not reside south of Canal Street, did not attend school south of Canal Street, and were not present south of Canal Street on the morning of 9/11.[18]

To enroll members of the WTCHR cohort in the present study, WTCHR staff of the New York City Department of Health (NYCDOHMH) who were fluent in English, Spanish, Mandarin, or Cantonese attempted contacts by mail, email, phone and in-person visits. Both a hard-copy letter and brochure describing the study were mailed to each potential participant. Two weeks after the mailing, phone calls were initiated to individuals who had not responded to the mailed invitation to participate. Calls were made to all known telephone numbers, and calls were attempted at different hours of the day and evening, and on different days of the week. Emails were sent to potential participants who did not respond to mail or telephone contacts. If there was no response to emails, then Lexis-Nexis (RELX Group: New York City, NY) search tools were used to identify new contact information. If new contact information was identified, then telephone and/or email contact were reinitiated. If no new contact information was obtained from tracing, two WTCHR staff members attempted a home visit to the last known place of residence. In all methods of contact, WTCHR staff described the study and invited individuals to call the WTCHR or NYU School of Medicine staff to further discuss study details and make an appointment. For participants less than 18 years of age a parent or guardian was required to schedule an

appointment and be available and present to authorize participation on the scheduled visit date.

For our comparison group, we recruited individuals who were not eligible for enrollment in the WTCHR. To maximize comparability between the two study populations we developed a table of the desired frequencies of controls by date of birth (0–2, 3–5 or ≥6 years-old on 9/11/2001), sex, race (White, African-American, Asian, other), ethnicity (Hispanic, non-Hispanic) and income (<$25,000, ≥$25,000), assuming that the enrolled group of WTCHR participants would reflect participants in the WTCHR's most recent (2011–12) survey cycle. Three modes of recruitment were employed to recruit the frequency-matched comparison group: (1) well visits at pediatric clinics affiliated with NYU School of Medicine; (2) contact through health fairs, youth organizations, and postings in areas where youth congregate, posting and advertisements at local colleges; and (3) social media outreach by West Coast Clinical Trials (WCCT) Global, a contract research organization. Participants' eligibility and ability to fill slots in the frequency-matching table were assessed using a screening questionnaire, which staff conducted over the phone or in person. Individuals were excluded from the present study as matched comparisons if they would have qualified for WTCHR enrollment because of place of residence or school, or having been in the vicinity of the WTC towers on 9/11/2001.

The study was reviewed and approved by the NYU School of Medicine Institutional Review Board, as well as research committees at Bellevue and Gouverneur Hospital Centers. The NYCDOHMH Institutional Review Board identified this study not to involve human subject activity by NYCDOHMH staff. In addition to parental consent on behalf of minors, assent was obtained from adolescents prior to initiation of the study procedures. A Certificate of Confidentiality was obtained to protect participant privacy. The study was approved by New York State Department of Health (NYSDOH) for the analysis of serum samples.

2.2 Sociodemographic and Exposure Variables

Demographic variables such as age, sex, race/ethnicity and family annual income (categorized as <$25,000 or ≥$25,000) were documented for each participant. Age groups were categorized as 0–2, 3–5 or ≥6 years old on 9/11/2001. Dust cloud (acute) and home dust (subchronic) exposure information was collected from both study participants and parent/guardian, if applicable. Dust cloud exposure was assessed categorically as present or absent with the question: "Were you caught in the WTC dust or debris cloud in the morning after the buildings collapsed on 9/11?" Home dust (subchronic) exposure was assessed categorically as present or absent with the question: "In the year after 9/11/01, did you live in an apartment or home in which WTC dust was visible on surfaces at any time, even if only briefly?" A positive response from either child or parent/guardian was used to indicate exposure.

In addition to dust exposure, psychosocially traumatic exposure was evaluated using an eight-item questionnaire developed by Hoven et al.[19] Presence of traumatic exposure was determined by a positive response to any of the following seven items either by parent or child: sight of either tower collapse, sight of injured people, sight of dead bodies, sight of

people falling out of buildings, physical injury to self, need to depart home/work for safety, and worry about safety of a loved one.

2.3 Anthropometric Measures & Dietary Data

We measured weight and height using calibrated stadiometers (Shorr Productions, Olney, MD) and scales (Seca model 881; Seca Corp., Hanover, MD), and calculated BMI as kg/m^2. Although current evidence indicates that dietary exposure to PFASs is highly unlikely to exceed health-based guidance values, [20] we decided to collect dietary data in recognition of diet as a possible source of exposure and differences between the two groups. Participants completed a web-based version of the Diet History Questionnaire II (DHQ II), which is a publicly available food frequency questionnaire (FFQ) developed by the National Cancer Institute. Of the four versions of the DHQ, participants completed the version that asks about diet in the past month, with portion size, which permits accurate and valid collection of caloric intake. The DHQ II benefits from validation in previous studies based upon an earlier version, confirming that it provides as good as or superior to the Willett and Block FFQs instruments for most nutrients.[21]

2.4 Serum Collection and Processing

Samples were collected from February 20, 2014 to March 21, 2016, and study visits were scheduled to occur after at least six hours of fasting. Following informed consent, blood, saliva, and urine samples were collected. Venipuncture collected 28.5 ml of which 15 mL was used to obtain serum. Serum was not obtained if participants chose to opt out of venipuncture. After collection, samples were immediately placed in cool storage and processed within three hours of collection time. Processed samples were then stored at −80°C until further analysis.

2.5 Measurement of PFASs

Eleven PFASs were measured in serum using a solid phase extraction (SPE) procedure and high-performance liquid chromatograph interfaced with an electrospray tandem mass spectrometer, using the methods similar to those described elsewhere.[22, 23] Internal standards for ^{13}C-labeled PFASs were added into serum samples prior to the addition of reagents for extraction.[24] Solvents, blood collection tubes, and method blanks (blinded to the laboratory) were tested for the presence of the PFASs. Target chemicals were not found in procedural blanks at concentrations above the limits of detection (LODs). The LODs of target chemicals ranged from 0.02 to 0.07 ng/mL. A standard reference material from the National Institute of Standards and Technology (NIST) was analyzed with every batch of 50 samples and recoveries of target chemicals were between 90 and 115% of the certified values. Recoveries of target chemicals passed through the entire analytical procedure ranged between 100 and 124%. Quantification was by isotope dilution and target chemicals were monitored by multiple reaction monitoring mode under negative ionization. The following PFASs were measured: PFHxS; n-methyl perfluorooctanesulfonamido acetic acid (N-meFOSAA); perfluorooctane sulfonamide (PFOSA); PFOS; perfluorodecanesulfonate (PFDS); perfluoroheptanoic acid (PFHpA); PFOA; perfluorononanoic acid (PFNA); perfluorodecanoic acid (PFDA); perfluoroundecanoic (PFUnDA); and perfluorododecanoic acid (PFDoDA).

2.6 Statistical Analyses

We conducted descriptive, univariate, and multivariate analyses with R Statistical Software (version 3.3.1). Chi-square testing was used to compare the two cohorts by sociodemographic and exposure variables. Caloric intake and serum PFASs were not normally distributed and therefore were compared between the two groups using the Wilcoxon Rank Sum test. PFAS concentrations were log-transformed to account for skewed distribution; following published practices, levels less than the LOD were imputed to be LOD/√2,[16] and we limited our statistical analyses to PFASs detected in ≥50% of the samples. Chi-square analyses also compared sociodemographic variables between WTCHR participants who were recruited for this study and WTCHR participants who were not.

Univariate analyses compared serum PFASs between WTCHR participants and matched comparisons, as well as by exposure variables. Correlation coefficients were also calculated for the three exposure variables. To avoid multicollinearity, separate multivariate models examined study arm; dust cloud; home dust; and traumatic exposures. All the multivariate regressions analyses controlled for: sex; race/ethnicity (White, African American, Asian, Other and Hispanic); age on September 11, 2001; and caloric intake (recognizing that diet can be a source of PFAS exposure).[25, 26] Variables were added to multivariate models if significant differences were identified between the two comparison groups at $p<0.1$.

2.7 Sensitivity Analysis

Since very young participants on the day of WTC attacks may have had limited recall of their actual exposures, sensitivity analyses were conducted to correct for potential recall bias. The sensitivity analyses considered results in which the child's age was <3 years old on 9/11/2001 as the cutoff for inclusion of child-reported exposures. We also performed a complete case analysis, excluding participants with missing income, and missing self-report of home dust, dust cloud or traumatic exposures.

3. Results

Participant flow diagrams for the WTCHR group and matched comparison are presented in the Appendix (Figures 1 and 2, respectively). Of the 222 matched comparisons, 185 (83.3%) provided serum for measurement of PFAS levels, while these were performed in 123 (68.3%) of the 180 WTCHR participants. Serum was not obtained if participants chose to opt out of venipuncture. Figure 1A and 1B shows boxplots of PFASs by exposure group and compares WTCHR participants to matched comparisons.

Comparisons were more likely to be female ($p=0.01$) and Hispanic, and less likely to be Asian ($p=0.04$) than WTCHR participants (Table 1). Caloric intake was also greater ($p=0.008$) in WTCHR than comparisons, supporting inclusion of caloric intake within multivariate models. Median caloric intake was more likely to be higher ($p=0.008$) in the WTCHR population (1709 calories) than the comparison group (1537 calories). Median PFOA (1.81 ng/mL) and PFOS (3.72 ng/mL) in the WTCHR group were approximately 2-fold less than the median identified among 12–19 year olds participating in the 2009–10 National Health and Nutrition Examination Survey (NHANES; 2.9 ng/mL for PFOA and 6.9

ng/mL for PFOS).[27] Six PFASs were detected in ≥50% of samples. No significant differences were detected between the two groups in terms of BMI category. (p=0.39). Despite our exclusion criteria, WTC exposures were also identified in the comparison group: 0.5% to dust cloud; 8.1% to home dust; and 43.2% for traumatic exposures. WTCHR participants were more Hispanic and less Asian (p=0.053) than the total eligible population of the WTCHR children (Appendix Table 1). WTCHR participants in our study were also more likely to have an annual income ≥$25,000 (p=0.0002) than nonparticipants eligible on the basis of WTCHR participation.

Univariate analyses revealed differences by study group for multiple PFASs. Belonging to the WTCHR group was associated with significantly higher levels of PFHxS (1.41% increase or 0.34 log unit increase, p<0.001); PFOS (1.31% increase or 0.27 log unit increase, p<0.001); PFOA (1.24% increase or 0.22 log unit increase, p<0.001); PFNA (1.25% increase or 0.22 log unit increase, p<0.001); PFDA (1.52% increase or 0.54 log unit increase, p<0.001); and PFUnDA (1.37% increase or 0.416 log unit increase, p=0.003) than participants in the comparison group (Table 2 and 3, univariate analyses). Univariate analyses also identified stronger associations of higher serum PFASs levels with subchronic, home dust exposure, than with acute, dust cloud exposure. Dust cloud exposure was significantly associated only with PFDA (1.61% increase or 0.47 log unit increase, p=0.005) and PFOA (1.15% increase or 0.14 log unit increase, p=0.037) levels. In contrast, home dust exposure and traumatic exposure were associated with PFOS, PFHxS, PFOA, and PFNA with increments similar to those found in association with WTCHR participation (Table 2 and 3, univariate analyses).

Moderate correlation was identified for all three-self-reported exposure variables (Appendix Table 2), supporting their separate examination in multivariate models. In these models we controlled for sex, caloric intake, race/ethnicity and date of birth group, and we detected significant increases among WTCHR participants compared with the matched comparison group (Table 2 and 3, multivariate analyses) for PFHxS (0.23 ng/mL increase or 0.24 log unit increase, p=0.006); PFOS (0.86 ng/mL increase or 0.16 log unit increase, p=0.011); PFOA (0.35 ng/mL increase or 0.18 log unit increase, p<0.001); PFNA (0.12 ng/mL increase or 0.17 log unit increase, p=0.003); PFDA (0.06 ng/mL increase or 0.42 log unit increase, p<0.001); and PFUnDA (0.03 ng/mL increase or 0.32 log unit increase, p=0.019). Multivariate models using self-reported exposures identified stronger associations between subchronic, home dust exposure with serum PFASs than with acute, dust cloud exposure. Dust cloud exposure was significantly associated only with PFDA (0.05 ng/mL increase or 0.51 log unit increase, p=0.001) and PFOA (0.24 ng/mL or 0.13 log unit increase, p=0.046). In contrast, home dust exposure was associated with PFOS, PFHxS, PFOA, PFNA, and PFDA with increments similar to those found by WTCHR participation. Multivariate analysis identified associations of traumatic exposures with PFOS, PFHxS, PFOA, PFNA, and PFUnDA (Table 2 and 3, multivariate analysis).

The sensitivity analyses revealed persistence of statistical significance for most associations of exposures with PFASs in the complete case analysis. Only the association of acute, dust cloud with PFOA (0.119 log unit increase, p=0.075; Appendix Table 3) and the associations of PFNA (0.11 log unit increase, p=0.13) and PFDA (0.22 log unit increase, p=0.13) with

subchronic home dust exposure attenuated in the complete analysis. The association of PFNA with traumatic exposures also attenuated to p=0.089 (0.116 log unit increase).

Sensitivity analysis that excluded reports of children who were <3 years old on September 11, 2001 revealed the same set of significant associations with dust cloud, WTCHR cohort, and traumatic exposure (Appendix Table 4). Significant associations also persisted for home dust, except for PFDA (0.22 log unit increase, p=0.085).

4. Discussion

In this study we detected an increase in serum PFASs among children exposed to the WTC disaster at <8 years of age and participating in the WTCHR compared to a sociodemographically matched group. The increases were concentrated among those who reported subchronic home dust exposure, traumatic exposures, and who were specifically a part of the WTCHR. The potential health implications of these results warrants further investigation and raise possible concerns about cardiometabolic outcomes among youth who were exposed in childhood.

Experimental studies have shown that PFASs activate alpha- and gamma-peroxisome proliferator activated receptors, [8–10] which play key roles in lipid and carbohydrate metabolism, providing biological plausibility for PFAS-induced childhood obesity and insulin resistance. A human study in children and adolescents has reported cardiometabolic and renal effects of childhood PFASs exposure.[28] Furthermore, PFASs have been associated with increases in serum uric acid in children ages 12–19 years enrolled in NHANES, and have been linked to reduced kidney function in children. [16] In addition, it has been reported that PFOS and PFNA concentrations were associated with lower levels of IGF-1 in children, [15] which, in turn, have been associated with metabolic syndrome[29] and increased risk of cardiovascular events in later life. [30]

We identified associations of traumatic exposures with PFOS, PFHxS, PFOA, PFNA, and PFUnDA, most likely reflecting proximity to the disaster site on September 11th and/or the following months. Current evidence indicates that traumatic exposure followed by post-traumatic stress disorder (PTSD) is associated with increased allostatic load resulting in significant physical and psychological morbidity. [31] PTSD has been associated with unhealthy behaviors such as increased alcohol use, smoking, increased caloric intake,[32] and with higher BMI and metabolic syndrome, [33] as well as new-onset diabetes in a WTC-exposed cohort. [34] It is therefore possible that the effects of traumatic exposures and higher concentrations of PFASs could act synergistically to increase cardiometabolic risk in this population.

Overall, identification of subpopulations vulnerable to WTC-associated cardiovascular effects could facilitate proactive interventions such as diet and lifestyle changes and, if necessary, treatment with antihypertensive medications which have been documented to prolong survival among adults with suboptimal cardiovascular profile.

Strengths of this study include: comparison of a group known to experience dust and traumatic exposures related to the disaster with a sociodemographically matched group;

valid and reliable biomonitoring methods; control for potential confounders; and evaluation of exposure by multiple methods including questionnaires of parent/guardian and child. Given that half-lives of PFASs range from 4–8 years[35] the detection of differences is striking and suggests even higher levels in exposed children in relation to the disaster. Comparison to the most recent naturally representative data from the 2009–10 National Health and Nutrition Examination Survey requires some care in that our sample (recruited between 2014 and 2015) is also likely to have been influenced by secular decreases which have been identified since 2009–10 given the recent phase out of multiple long-chain PFASs.[36, 37]

Although the WTCHR did collect multiple waves of exposure and health data by questionnaire, biospecimens from an earlier time point are not available. Given the long (12–14 year) time period between the disaster and study visits, we cannot rule out another source of exposure that would have otherwise explained the observed differences. Indeed, even though the comparison group had lower medians for all 6 PFASs compared to the WTCHR group (Table 1) we cannot exclude that individuals in the comparison group were also exposed to the dust cloud, or to home dust, although to a lesser extent. In addition, urban areas are recognized sources of PFASs to the environment, with PFOA identified as the predominant compound, accounting for >35% of the total PFAS concentrations, in all environmental matrices analyzed, [38] and we assume that these background levels of exposure can account for the levels detected in the comparison group. We also note the sex differences in our two samples, as well as the racial/ethnic differences, which were driven in disproportionate recruitment of non-Hispanic Asians for the WCTHR.

Other WTC chemical exposures have been previously examined in pregnant women. While these studies failed to detect differences in blood mercury[39] and polybrominated diphenyl ethers (PBDEs) among women living/working near the site, it should be noted that women in their second half of pregnancy on September 11, 2001 did have children with higher cord blood PBDE levels.[40] The unique relevance of our findings with those identified for PFASs could relate to differences in age of the study population, as persistent organic pollutants (POP) are known to accumulate over the lifespan,[41] resulting in greater baseline serum PBDEs before September 11, 2001 over which increments in PBDEs may have been more difficult to detect. Broader examinations of POPs in children are indicated, especially to dioxins, which have longer half-lives, [42] and are known to have been emitted in the wake of the disaster.[43]

Our findings also raise further questions about perinatally-acquired PFAS exposures resulting from the disaster, and potential consequences for adverse birth outcomes and later life cardiometabolic and renal dysfunction. PFOA levels in pregnant women have been related to increases in pregnancy-induced hypertension[44] and infants in the Norwegian Mother and Child Cohort study born with higher levels of PFASs were found to have slightly lower birth weight than those exposed to lower levels.[45] Another study identified lower weights among Danish infants exposed highly-exposed to PFASs *in utero* at ages 5 and 12 months compared to less exposed children, in a sex-dependent pattern.[46]

In conclusion, serum PFASs in this study were found to be higher in children enrolled in the WTCHR compared with levels detected in a matched comparison group of NYC residents.

Serum PFAS were also found to be higher in association with subchronic home dust exposures and traumatic exposures. These findings highlight the importance of conducting longitudinal studies to assess possible cardiometabolic and renal consequences related to these exposures.

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Abbreviations

BMI	Body Mass Index
HDL	High-density lipoprotein
LODs	Limits of Detection
N-MeFOSAA	N-methylperfluoro-1-octanesulfonamidoacetic acid
N-meFOSAA	N-methyl perfluorooctanesulfonamido acetic acid
NYSDOH	New York State Department of Health
NYC DOHMH	NYC Department of Health & Mental Hygiene
PFASs	Perfluoroalkyl substances
PFDS	Perfluorodecane sulfonate
PFDA	Perfluorodecanoic acid
PFDoDA	Perfluorododecanoic acid
PFHpA	Perfluoroheptanoic acid
PFHxS	Perfluorohexanesulfonic acid
PFNA	Perfluorononanoic acid
PFOSA	Perfluorooctane sulfonamide
PFOS	Perfluorooctanesulfonic acid
PFOA	Perfluorooctanoic acid

PFUnDA	Perfluoroundecanoic acid
WTC	World Trade Center
WTCHR	WTC Health Registry

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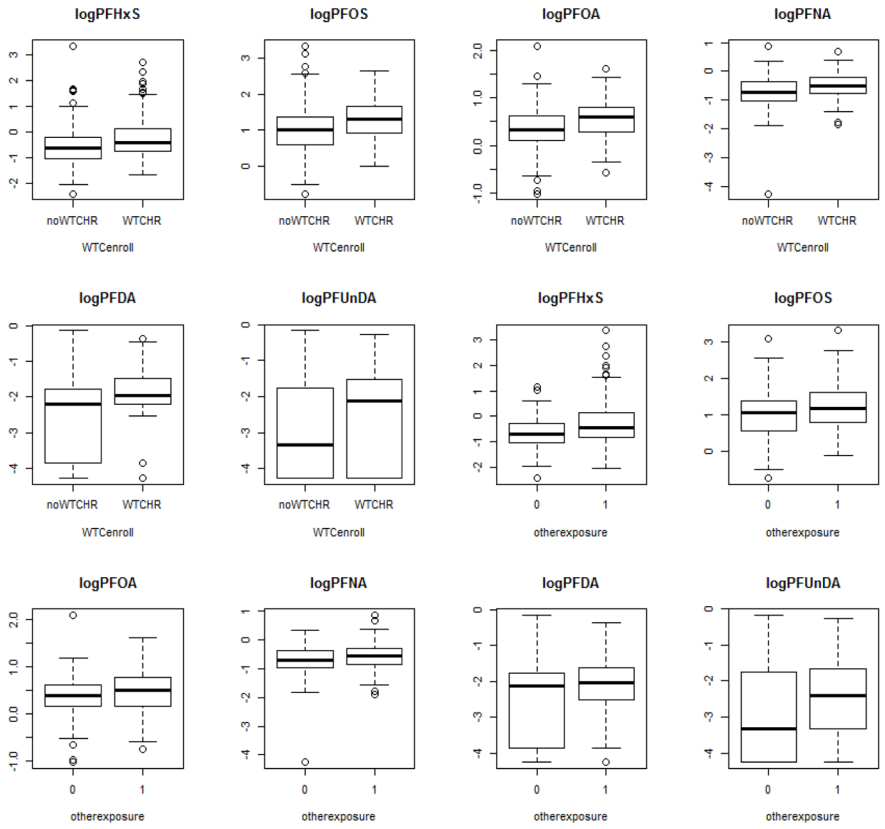
Highlights

- Perfluoroalkyl substances (PFASs) were released during the World Trade Center disaster
- PFAS levels were analyzed in serum of exposed youth and in a comparison group
- PFAS levels were higher in exposed participants
- Studies are needed to assess possible health consequences related to these exposures



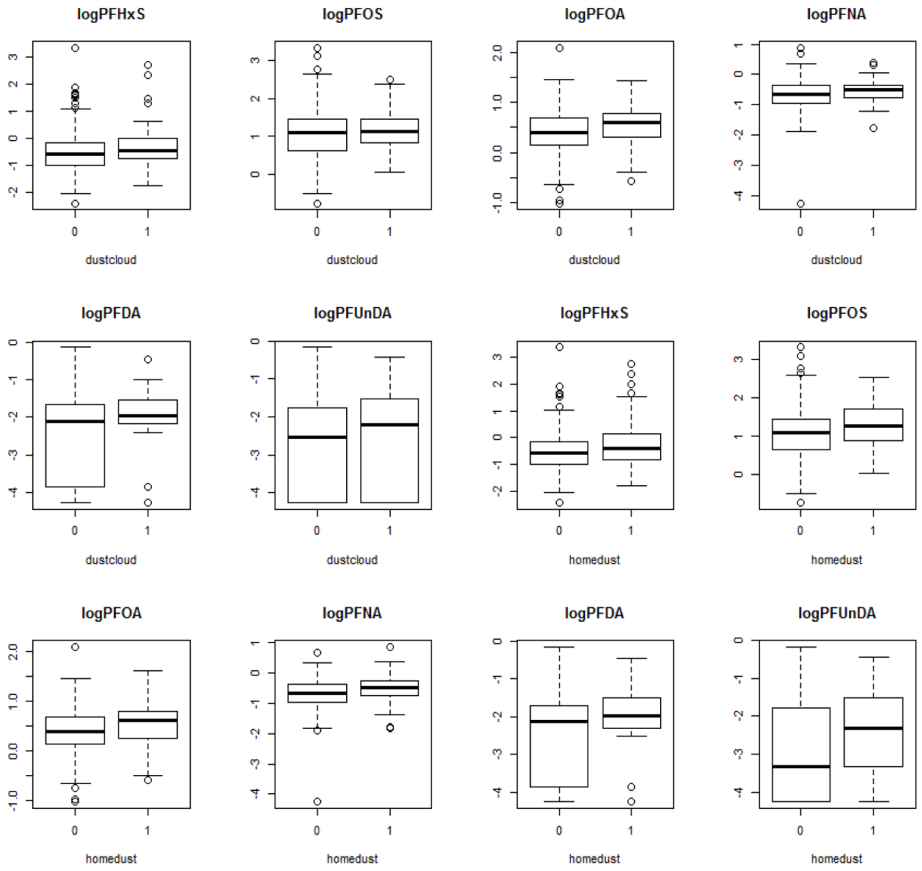
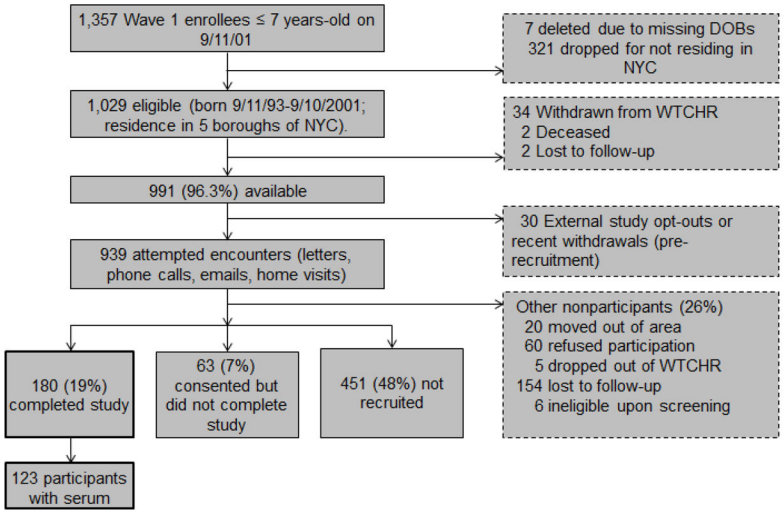
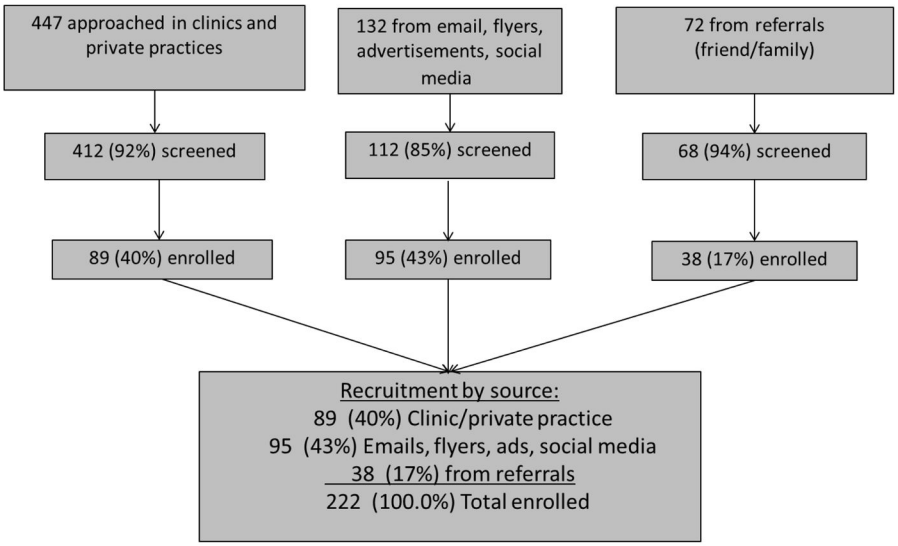


Figure 1.

A. Boxplots of Perfluoroalkyl Substances (PFASs, log units) in Serum of Children Exposed to World Trade Center Dust. *Legend:* otherexposure: traumatic exposures not related to the WTC disaster; noWTCHR: matched comparison group; WTCenroll: WTC Health Registry group. **B. Boxplots of Perfluoroalkyl Substances (PFASs, log units) in Serum of Children Exposed to World Trade Center Dust (Exposure to Dust Cloud and Home Dust).** *Legend:* noWTCHR: matched comparison group; WTCenroll: WTC Health Registry group



Appendix Figure 1.
Recruitment Flowchart for WTCHR Participants.



Appendix Figure 2.
Recruitment Flowchart for Matched Comparisons.

Table 1

Study Population Characteristics.

	308 samples		
	Comparison n=185	**WTCHR n=123**	**p value**
Sex			
Male	74 (40%)	69 (56.1%)	
Female	111 (60%)	54 (44.9%)	
Date of birth			
9/11/93–9/10/95	35 (18.9%)	34 (27.6%)	
9/11/95–9/10/98	73 (39.5%)	52 (42.3%)	**0.07**
9/11/98–9/10/01	77 (41.6%)	37 (30.1%)	
Income < $25,000 *	42 (22.7%)	19 (15.4%)	0.17
Race/Ethnicity ****			
Non-Hispanic White, %	72 (38.9%)	42 (34.4%)	
Non-Hispanic Black, %	17 (9.2%)	13 (10.7%)	
Non-Hispanic Asian, %	37 (20%)	30 (24.6%)	**0.04**
Non-Hispanic Other, %	6 (3.2%)	13 (10.7%)	
Hispanic	53 (28.6%)	24 (19.7%)	
Exposures ***			
Dust cloud exposure (%)	1 (0.5)	47 (43.9)	**<0.0001**
Home dust exposure (%)	15 (8.1)	69 (57)	**<0.0001**
Traumatic exposure (%)	80 (43.2)	109 (88.6)	**<0.0001**
Serum PFASs, ng/mL Median (IQR)			
PFHxS (n<LOD= 0 %)	0.53 (0.47)	0.67 (0.69)	**<0.0001**
PFOS (n<LOD= 0 %)	2.78 (2.18)	3.72 (2.82)	**<0.0001**
PFOA (n<LOD= 0 %)	1.39 (0.75)	1.81 (0.90)	**<0.0001**
PFNA (n<LOD= 0.3 %)	0.49 (0.33)	0.61 (0.36)	**<0.0001**
PFDA (n<LOD= 25 %)	0.11 (0.15)	0.14 (0.12)	**<0.0001**
PFUnDA (n<LOD= 47 %)	0.04 (0.16)	0.12 (0.21)	**0.007**
Calories, ** Median (IQR)	1537.39 (1014.41)	1708.75 (1317.49)	**0.008**
Body Mass Index Category			
Normal/Underweight	137 (74.1)	98 (79.7)	0.387
Obese	20 (16.3)	8 (4.3)	
Overweight	28 (15.1)	17 (13.8)	

* n=38 missing for comparison; n=27 missing for WTCHR

** n=2 missing for caloric intake

*** n=18 missing for dust cloud exposure; n=2 missing for home dust exposure

**** n=1 missing for race/ethnicity

Table 2

Comparisons of Serum PFASs by Exposure Characteristics.

Univariate	Dust cloud		Home dust		Traumatic Exposure		WTCHR	
PFASs	**log unit increase (95% CI)**	**p value**	**log unit increase (95% CI)**	**p value**	**log unit increase (95% CI)**	**p value**	**log unit increase (95% CI)**	**p value**
PFHxS	0.216 (−0.03, 0.462)	0.085	0.263 (0.063, 0.464)	**0.01**	0.359 (0.179, 0.54)	**<0.001**	0.342 (0.163, 0.522)	**<0.001**
PFOS	0.078 (−0.107, 0.263)	0.407	0.187 (0.036, 0.337)	**0.015**	0.193 (0.056, 0.33)	**0.006**	0.271 (0.136, 0.405)	**<0.001**
PFOA	0.144 (0.009, 0.28)	**0.037**	0.169 (0.059, 0.28)	**0.003**	0.111 (0.009, 0.212)	**0.032**	0.218 (0.119, 0.316)	**<0.001**
PFNA	0.13 (−0.031, 0.292)	0.113	0.175 (0.046, 0.305)	**0.008**	0.124 (0.005, 0.242)	**0.041**	0.224 (0.108, 0.34)	**<0.001**
PFDA	0.476 (0.145, 0.807)	**0.005**	0.269 (−0.002, 0.539)	0.051	0.193 (−0.054, 0.44)	0.125	0.536 (0.297, 0.776)	**<0.001**
PFUnDA	0.210 (−0.165, 0.584)	0.271	0.286 (−0.018, 0.59)	0.065	0.265 (−0.014, 0.543)	0.062	0.416 (0.142, 0.691)	**0.003**
Multivariate[+]	**Dust cloud**		**Home dust**		**Traumatic Exposure**		**WTCHR**	
PFASs	*log unit increase (95% CI)*	*p value*	*log unit increase (95% CI)*	*p value*	*log unit increase (95% CI)*	*p value*	*log unit increase (95% CI)*	*p value*
PFHxS	0.108 (−0.12, 0.336)	0.353	0.236 (0.052, 0.419)	**0.012**	0.253 (0.08, 0.426)	**0.004**	0.241 (0.07, 0.411)	**0.006**
PFOS	0.069 (−0.096, 0.234)	0.412	0.184 (0.053, 0.315)	**0.006**	0.125 (0, 0.25)	**0.05**	0.159 (0.036, 0.281)	**0.011**
PFOA	0.125 (0.002, 0.248)	**0.046**	0.159 (0.06, 0.258)	**0.002**	0.104 (0.01, 0.199)	**0.03**	0.178 (0.086, 0.269)	**<0.001**
PFNA	0.126 (−0.026, 0.278)	0.103	0.159 (0.038, 0.28)	**0.01**	0.119 (0.004, 0.234)	**0.043**	0.168 (0.056, 0.28)	**0.003**
PFDA	0.507 (0.205, 0.809)	**0.001**	0.25 (0.004, 0.496)	**0.046**	0.161 (−0.073, 0.395)	0.177	0.421 (0.195, 0.647)	**<0.001**
PFUnDA	0.263 (−0.086, 0.611)	0.139	0.279 (−0.001, 0.558)	0.051	0.288 (0.02, 0.555)	**0.035**	0.315 (0.053, 0.578)	**0.019**

(+): Each column represents an examination of a single exposure variable or study arm controlled for sex, caloric intake, race/ethnicity and Date of Birth group.

Table 3

Comparisons of Serum PFASs by Exposure Characteristics (Reported as Percent Change and Increase in ng/mL)

	Dust cloud			Home dust			Traumatic Exposure			WTCHR		
PFASs	**Percent change (univariate) (95% CI)**	**Percent change (multivariate) (95% CI)**	**Unit increase (ng/mL)**	**Percent change (univariate) (95% CI)**	**Percent change (multivariate) (95% CI)**	**Unit increase (ng/mL)**	**Percent change (univariate) (95% CI)**	**Percent change (multivariate) (95% CI)**	**Unit increase (ng/mL)**	**Percent change (univariate) (95% CI)**	**Percent change (multivariate) (95% CI)**	**Unit increase (ng/mL)**
PF Hx S	1.24 (0.97, 1.59)	1.11 (0.89, 1.4)	0.15	1.3 (1.07, 1.59)	1.27 (1.05, 1.52)	0.18	1.43 (1.2, 1.72)	1.29 (1.08, 1.53)	0.22	1.41 (1.18, 1.69)	1.27 (1.07, 1.51)	0.23
PF OS	1.08 (0.9, 1.3)	1.07 (0.91, 1.26)	0.24	1.21 (1.04, 1.4)	1.2 (1.05, 1.37)	0.6	1.21 (1.06, 1.39)	1.13 (1, 1.28)	0.59	1.31 (1.15, 1.5)	1.17 (1.04, 1.32)	0.86
PF OA	1.15 (1.01, 1.32)	1.13 (1, 1.28)	0.24	1.18 (1.06, 1.32)	1.17 (1.06, 1.29)	0.27	1.12 (1.01, 1.24)	1.11 (1.01, 1.22)	0.17	1.24 (1.13, 1.37)	1.19 (1.09, 1.31)	0.35
PF NA	1.14 (0.97, 1.34)	1.13 (0.97, 1.32)	0.07	1.19 (1.05, 1.36)	1.17 (1.04, 1.32)	0.09	1.13 (1.01, 1.27)	1.13 (1, 1.26)	0.07	1.25 (1.11, 1.4)	1.18 (1.06, 1.32)	0.12
PF DA	1.61 (1.16, 2.24)	1.66 (1.23, 2.25)	0.05	1.31 (1, 1.71)	1.28 (1, 1.64)	0.02	1.21 (0.95, 1.55)	1.17 (0.93, 1.48)	0.02	1.71 (1.35, 2.17)	1.52 (1.22, 1.91)	0.06
PF Un DA	1.23 (0.85, 1.79)	1.3 (0.92, 1.84)	0.02	1.33 (0.98, 1.8)	1.32 (1, 1.75)	0.02	1.3 (0.99, 1.72)	1.33 (1.02, 1.74)	0.02	1.52 (1.15, 2)	1.37 (1.05, 1.78)	0.03

Appendix Table 1

Comparison of world trade center health registry (WTCHR) participants to other eligible individuals who did not take part in the WTCHR

	WTCHR Study (n=123)	Nonparticipants (n=816)	p value
Male, %	56.1%	50.4%	0.28
Date of Birth			
9/11/93-9/10/95	27.6 %	34.7 %	**0.08**
9/11/95-9/10/98	42.3%	43.9%	
9/11/98-9/10/01	30.1%	21.4%	
Income < $25,000 **	19.8%	40.2%	**0.0002**
Race/Ethnicity ***			0.053
Non-Hispanic White	34.4%	46.6%	
Non-Hispanic Black	10.7%	5.8%	
Asian	24.6%	22.4%	
Other	10.7%	7.4%	
Hispanic or Latino	19.7%	18.0%	

** income missing for n=27 participants and 102 nonparticipants

*** race/ethnicity missing for n=1 participants

Appendix Table 2

Pearson Correlation Coefficients of Exposure Variables

	Home Dust	Dust Cloud	Traumatic Exposure
Home Dust		0.50 *	0.30 *
Dust cloud			0.37 *
Traumatic Exposure			

* p<0.001

Appendix Table 3

Complete Cases - Univariate and Multivariate Analyses.

Univariate	Dust cloud		Home dust		Traumatic Exposure		WTCHR	
PFASs	**log unit increase (95% CI)**	**p value**	**log unit increase (95% CI)**	**p value**	**log unit increase (95% CI)**	**p value**	**log unit increase (95% CI)**	**p value**
PFHxS	0.227 (−0.021, 0.476)	0.073	0.269 (0.067, 0.472)	**0.009**	0.375 (0.198, 0.553)	**<0.00 1**	0.342 (0.163, 0.522)	**<0.001**
PFOS	0.072 (−0.114, 0.259)	0.445	0.177 (0.025,0.33)	**0.023**	0.235 (0.1,0.369)	**0.001**	0.271 (0.136,0.405)	**<0.001**
PFOA	0.138 (0.001,0.275)	**0.049**	0.158 (0.046,0.27)	**0.006**	0.122 (0.022,0.222)	**0.017**	0.218 (0.119,0.316)	**<0.001**
PFNA	0.126 (−0.036,0.289)	0.127	0.156 (0.024,0.287)	**0.02**	0.16 (0.043,0.277)	**0.007**	0.224 (0.108,0.34)	**<0.001**
PFDA	0.473 (0.139,0.807)	**0.006**	0.239 (−0.035,0.513)	0.088	0.279 (0.036,0.523)	**0.025**	0.536 (0.297,0.776)	**<0.001**
PFUnDA	0.197 (−0.18,0.575)	0.305	0.237 (−0.071,0.545)	0.132	0.328 (0.053,0.602)	**0.019**	0.416 (0.142,0.691)	**0.003**
Multivariate[¥]	**Dust cloud**		**Home dust**		**Traumatic Exposure**		**WTCHR**	
PFASs	*log unit increase (95% CI)*	*p value*	*log unit increase (95% CI)*	*p value*	*log unit increase (95% CI)*	*p value*	*log unit increase (95% CI)*	*p value*
PFHxS	0.16 (−0.081,0.401)	0.193	0.204 (0.005,0.404)	**0.045**	0.27 (0.086,0.454)	**0.004**	0.242 (0.055,0.429)	**0.011**
PFOS	0.135 (−0.041,0.31)	0.133	0.2 (0.056,0.343)	**0.007**	0.165 (0.03,0.299)	**0.017**	0.22 (0.085,0.354)	**0.001**
PFOA	0.119 (−0.012,0.249)	0.075	0.137 (0.027,0.246)	**0.014**	0.121 (0.018,0.223)	**0.021**	0.171 (0.069,0.273)	**0.001**
PFNA	0.1 (−0.074,0.274)	0.259	0.111 (−0.032,0.254)	0.128	0.116 (−0.018,0.249)	0.089	0.149 (0.015,0.282)	**0.03**
PFDA	0.607 (0.264,0.949)	**0.001**	0.219 (−0.068,0.505)	0.134	0.225 (−0.042,0.492)	0.098	0.487 (0.224,0.751)	**<0.001**
PFUnDA	0.232 (−0.159,0.623)	0.244	0.274 (−0.045,0.592)	0.092	0.312 (0.013,0.61)	**0.041**	0.301 (0, 0.603)	**0.05**

[¥]Each column represents multivariable analysis controlled for sex, caloric intake, race/ethnicity and date of birth group. The models examined exposure variable and study arm separately.

Appendix Table 4

Sensitivity Analysis Excluding Reports of Participants <3 years old on the day of WTC Attacks.

Multivariate[¥]	Dust cloud		Home dust		Traumatic Exposure		WTCHR	
PFASs	**log unit increase (95% CI)**	**p value**	**log unit increase (95% CI)**	**p value**	**log unit increase (95% CI)**	**p value**	**log unit increase (95% CI)**	**p value**
PFHxS	0.126 (−0.104,0.356)	0.283	0.25 (0.065,0.435)	**0.008**	0.266 (0.092,0.441)	**0.003**	0.241 (0.07,0.411)	**0.006**
PFOS	0.066 (−0.1, 0.232)	0.437	0.171 (0.038, 0.304)	**0.012**	0.147 (0.021, 0.273)	**0.022**	0.159 (0.036, 0.281)	**0.011**
PFOA	0.126 (0.002, 0.249)	**0.047**	0.154 (0.054, 0.254)	**0.003**	0.108 (0.013, 0.203)	**0.027**	0.178 (0.086, 0.269)	**<0.001**
PFNA	0.127 (−0.026, 0.281)	0.102	0.142 (0.019, 0.264)	**0.023**	0.153 (0.037, 0.268)	**0.01**	0.168 (0.056, 0.28)	**0.003**
PFDA	0.508 (0.203, 0.812)	**0.001**	0.218 (−0.031, 0.467)	0.085	0.219 (−0.017, 0.455)	0.069	0.421 (0.195, 0.647)	**<0.001**
PFUnDA	0.248 (−0.103, 0.6)	0.165	0.22 (−0.063, 0.502)	0.127	0.325 (0.056, 0.595)	**0.018**	0.315 (0.053, 0.578)	**0.019**

[¥]Each column represents multivariable analysis controlled for sex, caloric intake, race/ethnicity, and date of birth group. The models examined exposure variable and study arm separately.